INTERMEDIATE-TERM RESULTS AFTER EN BLOC DOUBLE-LUNG TRANSPLANTATION WITH BRONCHIAL ARTERIAL REVASCULARIZATION

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***Objective*: Between May 1990 and January 1994, 18 patients underwent en bloc double-lung transplantation with tracheal anastomosis and bronchial arterial revascularization. Because at that time it was already suggested that chronic ischemia could be a contributing factor in occurrence of obliterative bronchiolitis, the purpose of this study was to evaluate, with a follow-up ranging from 22 to 69 months, the midterm effects of bronchial arterial revascularization on development of obliterative bronchiolitis. *Results*: Results were assessed according to tracheal healing, functional results, rejection, infection, and incidence of obliterative bronchiolitis. There were no intraoperative deaths or reexplorations for bleeding related to bronchial arterial revascularization, but there were three hospital deaths and five late deaths, two of them related to obliterative bronchiolitis. According to the criteria previously defined, tracheal healing was assessed as grade I, IIa, or IIb in 17 patients and grade IIIa in only one patient. Early angiography (postoperative days 20 to 40) demonstrated a patent graft in 11 of the 14 patients in whom follow-up information was obtained. Ten patients are currently alive with a 43-month mean follow-up. Among the 15 patients surviving more than 1 year, functional results have been excellent except in five in whom obliterative bronchiolitis has developed and who had an early or late graft thrombosis. Furthermore, those patients had a significantly higher incidence of late acute rejection ($p < 0.02$), cytomegalovirus disease ($p < 0.006$), and bronchitis episodes ($p < 0.0008$) than patients free from obliterative bronchiolitis. *Conclusion*: We conclude that besides its immediate beneficial effect on tracheal healing, long-lasting revascularization was, at least in this small series, associated with an absence of obliterative bronchiolitis, thus suggesting but not yet proving the possible role of chronic ischemia in this multifactorial disease. (J Thorac Cardiovasc Surg 1996;112:1292-300)**

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The advantages and feasibility of restoring the bronchial arterial circulation in lung transplantation to improve airway healing was demonstrated as early as 1950 by Métras[1] and was confirmed in animal experiments in 1970 by Mills, Boyd, and Gheranpong.[2] In 1990, Schreinemakers and associates[3] pointed out, in a both provocative and good sense aphorism, that "it makes as much sense to transplant lungs without bronchial arteries as to transplant hearts without coronary arteries." Cooper had concluded this discussion hoping that "restoration of bronchial circulation could become a routine part of single-lung, double-lung, and heart-lung transplantation."[3] In fact, in the early days of clinical lung transplantation, the significant morbidity and mortality related to airway ischemia[4] confirmed that the lack of blood supply was harmful and

responsible for these dreadful complications. However, bilateral lung transplantation remained a necessary therapeutic option for patients with septic end-stage lung diseases; because airway complications were less likely to occur in heart-lung transplantation, this option was chosen when a bilateral transplant was needed. Nevertheless, since 1986, because of the shortage of heart-lung block donors and the need to use the heart alone for another recipient, the surgical technique of double-lung transplantation (DLT) has evolved. Many techniques were developed to prevent ischemia,[5] such as wrapping the airway anastomosis with omental and mediastinal flaps. More recently, some authors introduced alternative techniques such as sequential DLT with bronchial anastomosis,[6] and for the same reason, other groups initiated single-lung transplantation with contralateral pneumonectomy.[7] At last, improvement in organ preservation and techniques for bronchial anastomosis, as well as a better management of immunosuppression and rejection surveillance, have considerably reduced the prevalence of airway complications.[8]

Despite a dramatic improvement in the immediate results of lung transplantation, however, the occurrence of obliterative bronchiolitis (OB) remains the most feared complication. It represents, at midterm and long-term follow-up, an obvious failure of lung transplantation.[9] Alloimmune responses, rejection, and infection episodes have been demonstrated to be of fundamental importance in the pathogenesis of OB,[10] but the devascularization and consequently the chronic ischemia of the tracheobronchial tree could be a nonnegligible contributing factor. For this reason, after anatomic and angiographic studies of the tracheobronchial arterial blood supply,[3, 11, 12] we developed in 1990 a simple technique of bronchial arterial revascularization for en bloc DLT with tracheal anastomosis. Our first results in eight patients with a mean follow-up of 11 months were reported in 1992.[13] But this too short follow-up did not allow us to assess whether bronchial arterial revascularization could have some beneficial impact in decreasing the incidence of OB. The purpose of this study is thus to evaluate, with a longer follow-up, the possible effect of revascularization on OB occurrence.

Patients and methods

Between May 1990 and January 1994, 18 patients underwent en bloc DLT with tracheal anastomosis and bronchial arterial revascularization in the Department of Thoracic Surgery at Xavier Arnozan Hospital. There were 13 male and five female patients with a mean age of 43.6 ± 11.9 years (range 16 to 63 years). Indications for DLT were chronic obstructive pulmonary disease in nine patients, of whom two had an α_1-antitrypsin deficiency, cystic fibrosis in one, and pulmonary fibrosis in eight patients, for whom DLT was preferred because of recurrent infectious complications. All these patients, dependent on supplemental oxygen were in New York Heart Association functional class III (38.9%) or IV (61.1%). All the donor organs but four were from local procurement, and for all the recipients but one, the graft was ABO identical.

Operative technique for donor lung harvesting, organ preparation, recipient operation, and organ implantation, as well as the revascularization procedure, have been previously described.[12, 13] The main steps of the technique are designed to preserve the right intercostobronchial artery or a common bronchial arterial trunk supplying the right and left main bronchi, as well as the periesophageal and subcarinal network. Consequently, so that these collateral networks supplying both bronchi will not be disrupted, the orifice of the right intercostobronchial artery is not mobilized as a pedicle, but left in place in the posterior mediastinum. Thus the procedure for revascularization used a saphenous vein graft interposed between the orifices of the bronchial arteries and the recipient's ascending aorta. Tightness and runoff of the distal anastomosis can be checked before implantation of the double-lung block by flushing heparinized saline solution into the venous graft.

Standard immunosuppression consisted of cyclosporine, steroids, azathioprine, and antilymphocyte antibody. Cyclosporine was given as a continuous infusion (3 mg/kg) at the beginning of the operation, followed by enteral administration. The dose was adjusted to obtain a blood level between 150 and 250 ng/ml. Methylprednisolone was administered intravenously (500 mg) during the transplantation and followed by oral prednisolone (1 mg/kg per day) quickly tapered to 0.2 mg/kg per day. A 5-day course of intravenous prostacyclin (Flolan, Burrows Wellcome Co., Research Triangle Park, N.C.) was given in seven of 18 patients. All the patients but three (cytomegalovirus seronegative receiving a seronegative graft) had 8 to 21 days of prophylaxis with ganciclovir (Cimevan, Roche Laboratories, Nutley, N.J.). All the patients had the same antibacterial prophylaxis with imipenem and ciprofloxacine for 5 days, and trimethoprin sulfamethoxazole was given until the fifteenth postoperative day to prevent *Pneumocystis carinii* infection.

A flexible fiberoptic bronchoscope was used almost every day during the first week for bronchial aspirations and analyses and then routinely twice a week or when dictated by clinical parameters. Bronchoscopy with photographs was performed between days 15 and 20 to assess tracheal healing according to the classification previously described.[14]

Baseline venous graft angiography was performed between the third and fourth weeks after the transplantation. Long-term patency was also assessed by angiography in seven living patients in whom the graft was initially

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Table I. *Early comparative assessment of tracheal healing and venous graft patency*

Tracheal healing			*Venous graft baseline angiography*		
	Patients			*Patent*	
Grade	*No.*	*%*	*No. of grafts*	*No.*	*%*
I	7	38.9	5	5	100
IIa	7	38.9	6	3	50
IIb	3	16.6	2	2	100
III	1	5.6	1	1	100
Total	18	100	14	11	78.6

patent or not evaluated in the early posttransplantation period.

The pulmonary functional status was evaluated by the usual parameters, which included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), forced expiratory flow rate between 25% and 75% of the forced vital capacity ($FEFR_{25/75}$), and arterial oxygen tension (Pao_2) and carbon dioxide tension ($Paco_2$) in millimeters of mercury.

For purposes of this review, pneumonia was defined as associating clinical symptoms, radiographic findings, and isolation of the pathogen in the lung, whereas episodes of bronchitis were defined as clinical symptoms with isolation of the pathogen in the bronchial tree, without radiographic abnormalities. With regard to cytomegalovirus (CMV), biologic infection was defined as a positive viremia or the discovery of the virus in the bronchoalveolar lavage without clinical symptoms, and CMV disease was defined as the association of clinical symptoms, radiographic abnormalities, and the presence of the virus in a tissue. Rejection was diagnosed on the basis of transbronchial lung biopsy histology by means of the International Classification[15] or on clinical and paraclinical findings with a good response to specific treatment. As recommended in the literature, we have opted for the International Classification of Bronchiolitis Obliterans Syndrome.[16]

Infection was treated with specific antimicrobial agents. Acute rejection was treated with a 3-day bolus methylprednisolone course (1 gm dose) or with OKT3 for 10 days in the event of any resistant or persistent rejection. CMV biologic infections or diseases were treated with a 15-day course of ganciclovir. All the patients with OB had an increase in immunosuppression at the very least.

With regard to statistical analysis, data are expressed as mean plus or minus 1 standard deviation. Actuarial survival was calculated with the Kaplan-Meier method. Paired t test was used to evaluate the differences over time within all patients for the respiratory parameters. Significance was sought between the two groups of patients with and without OB with the use of χ^2 test for nonparametric data and Student's t test for continuous data. Statistical significance was accepted at the 95% confidence level, $p < 0.05$.

Results

Early events. Three patients required reexploration for early bleeding related to previous pleural adhesions, but there was no bleeding related to bronchial arterial revascularization. There was no intraoperative death, and all patients but two were extubated in a mean of 1.9 days (range 12 hours to 4 days).

Tracheal healing. All 18 patients had bronchoscopy to assess tracheal healing. Staging results are shown in Table I. According to our classification,[14] 17 patients (94.4%) had grade I or II healing, and no late stenosis was observed in patients discharged from the hospital. Grade IIIa was assessed in only one patient, without subsequent complication. Therefore no early tracheal dehiscence was detected in these patients.

Hospital mortality. There were three hospital deaths (16.6%). Among the patients who died were the two who could not be weaned from the ventilator. The first one, a 56-year-old man with emphysema and alveolar proteinosis, ventilator-dependent before transplantation, died on postoperative day 16 of multiorgan failure. However, there was no graft dysfunction and tracheal healing was excellent. The second patient, a 63-year-old woman, died on postoperative day 51 of cataclysmic hemoptysis. On postoperative day 15 tracheal healing was classed as grade I, but bronchial necrosis subsequently developed with severe infection (*Pseudomonas aeruginosa* and *Aspergillus fumigatus*) and severe steroid-resistant acute rejection treated with OKT3. She soon required tracheotomy and stenting of the main bronchus for severe distal malacia. The hemorrhage was probably due to vascular erosion and rupture in relation with the Gianturco stent. This death was obviously related to an airway complication, as defined by Date and associates,[8] but the respective responsibility of necrotizing infection and of a probable ischemia, despite adequate tracheal healing, remained questionable. The third patient, a 35-year-old man with paraquat poisoning, had an uneventful immediate postoperative course, but he died 35 days later of massive intestinal hemorrhage.

Early venous graft patency. Only three of the 14 patients undergoing early baseline angiography had a graft occlusion at the time of the angiogram but nevertheless had grade IIa tracheal healing (Table I). The 11 other patients had a patent venous graft with a good runoff in the bronchial circulation. Therefore the early patency rate in these 14 patients was 78.6%.

Morbidity. Follow-up of the 15 patients discharged from the hospital ranged from 22 to 69 months. The main events in these patients are shown in Table II. Four patients did not have any episode of rejection; almost all episodes of rejection were successfully treated by methylprednisolone pulses except in two patients who required OKT3. Recipient and donor were not matched for the CMV. Thirteen patients were seropositive before transplantation and received a seropositive ($n = 6$) or a seronegative ($n = 7$) graft. Five recipients were seronegative and four of them received a seronegative donor block. Active CMV diseases have developed in half of the patients. The site of infection was pulmonary in eight cases, gastrointestinal in two, and ocular in one. The most frequent complications were episodes of bronchitis or pneumonia. The causal agent was bacteria, a virus other than CMV, or fungi. A pleuropulmonary tuberculosis developed 4 months after transplantation in one patient and responded well to drugs.

Late deaths and actuarial survival. Five patients had died by the last date of follow-up, at a mean delay of 570 days (range 324 to 1493 days). Causes of death were scleroderma fibrosis relapse in one patient, sepsis and end-stage renal failure in two others, and OB in two patients. Consequently, the actuarial patient survival including hospital mortality was, at 1, 2, and 5 years, 77.8% ± 0.9%, 72.2% ± 1.5%, and 46.9% ± 1.3%, respectively.

Functional results. In the 15 surviving patients, pulmonary function parameters improved dramatically as early as 1 month after the transplantation (Fig. 1). FVC remained stable over time between 70% and 90% of predicted values. Of the two other parameters, $FEFR_{25/75}$ was the first to decrease, just before FEV_1. These alterations were due to OB occurrence. But despite FEFR and FEV_1 decrease, arterial blood gas analysis remained within normal limits, with a mean Pao_2 over 75 mm Hg and a normal $Paco_2$ (Fig. 2).

OB incidence. Of the 15 patients with a follow-up ranging from 22 to 69 months (mean 43 months), five patients (33%) have had clinical and functional features of OB in a mean interval of 19.2 ± 9 months. One patient had stage 3a OB and four had stage 3b. The histologic diagnosis of OB was proved by surgical biopsy in two patients, transbronchial biopsies in one, and autopsy in another one. We failed to prove OB in the last patient who had only the clinical and functional features. The treatment of OB in all five patients consisted of augmentation of immunosuppression. Of these, two died. One patient recovered and now lives a nearly normal life. Another one requires supplemental oxygen, is not ambulatory, and is waiting for a second transplant. The last patient underwent retransplantation 26 months ago and is currently well. In none of these patients we did find any relationship of OB with human leukocyte antigen (HLA), except that all patients with OB had two mismatches on the HLA locus A and all but one also had two mismatches on HLA locus DR.[17]

Table II. *Number of early and late acute rejections, CMV infections and diseases, and other infectious episodes*

Event	*No. per patient*
Acute rejection (<3 mo)	1 ± 0.97
Acute rejection (>3 mo)	0.50 ± 0.6
CMV infection	1.28 ± 1.18
CMV disease	0.78 ± 1.06
Bronchitis	2.8 ± 2.4
Pneumonia	1.3 ± 1.08

Data are mean ± standard deviation. *CMV,* Cytomegalovirus.

Because we hoped that bronchial revascularization could help to prevent OB, the variables listed in Table III were compared between the 10 patients free from OB (group 1) and the five patients with OB (group 2). With a mean follow-up of 34.5 months in group 1 versus 47.2 months in group 2, there was no statistically significant difference among the following seven variables: recipient and donor age, donor stay in the intensive care unit, cold ischemic time, bypass time, duration of mechanical ventilation, and incidence of early acute rejection. In addition, there was no difference between the two groups for HLA matching. With regard to late acute rejection, CMV disease, bronchitis, and total infection episodes, however, there was a striking and highly significant difference between the two groups. These events were considerably less prevalent in patients free from OB. Moreover, the late graft patency associated with long-lasting bronchial revascularization was 71.4% in group 1 and 0 in group 2. Consequently, despite the small number of patients in this series, and without asserting any connection between cause and effect, the relation between graft patency, OB incidence, and late rejection and infection episodes can only be pointed out. However, statistical analysis of bronchial arterial revascularization is missing, because this report is a retrospective study, and because all the data on the grafts

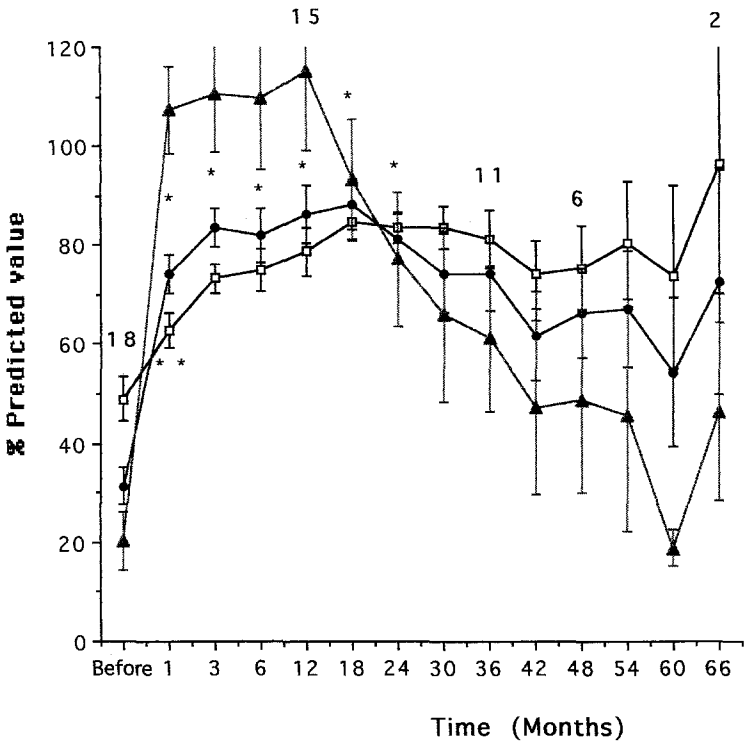

Fig. 1. Pulmonary function parameters over time. The parameters studied were FVC (□), FEV_1 (●), and $FEFR_{25/75}$ (▲) expressed as percentage of the predicted value. Each *point* represents the mean value ± standard error of the mean. Parameters are given before transplantation, at 1, 3, and 6 months, and then every 6 months. Figures represent the number of patients evaluated at each time. $^*p < 0.0001$: comparison between the parameters (FEV_1 and $FEFR_{25/75}$) before transplantation and at 1, 6, and 12 months after transplantation). $^{**}p < 0.05$: comparison between FVC before transplantation and after 1 month.

were not available. Some patients had an early patent graft, but died without OB and without a late graft evaluation. Nevertheless, all the patients with OB had graft thrombosis either early or late.

Discussion

To date, for most of the authors, indications for en bloc DLT remain questionable because the need for airway revascularization is controversial.[18] For that reason and because of the attendant complexity of bronchial arterial revascularization, this technique has not been widely adopted by other transplant groups. When bilateral lung transplantation is needed, most groups performed DLT with distal and telescoping bronchial anastomosis, sequential DLT, and pharmacologic agents.[19] A recent report by Date and associates[8] on a large series of single-lung and double-lung transplants with bronchial anastomosis demonstrated that the prevalence of airway complications was reduced by the conjunction of many factors. However, when tracheal anastomosis is performed, restoration of tracheobronchial blood supply is mandatory. By comparison with the early reports on airway complications after DLT with tracheal anastomosis,[4] our incidence of airway complication is 5.5% (1/18 patients), and there was neither early dehiscence nor late stricture in the surviving patients. In addition, except for the one death related to airway complications, no other early or late death could be attributable to the technique itself. With regard to bronchial arterial revascularization, some groups[20-22] using the internal thoracic artery maintain that bronchial revascularization remains useful for lung transplantation. The excellent results reported by Daly and associates[20] for single-lung and by Pettersson and colleagues[21] for en bloc DLT with tracheal anastomosis have proved that associated revascularization was a well-founded and sound policy, at least for the immediate aim of providing a satisfactory bronchial or tracheal healing. But what-

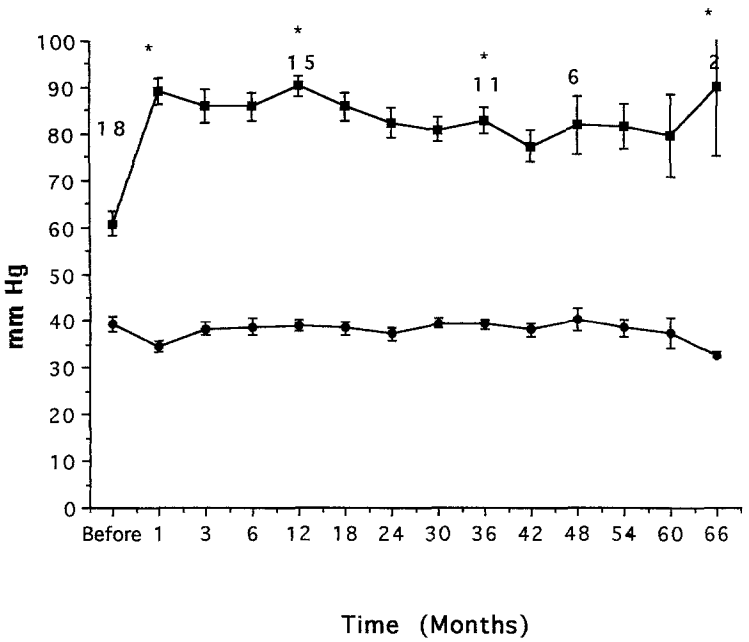

Fig. 2. Evolution of arterial blood gases over time. The parameters studied were Pao_2 (■) and $Paco_2$ (●), expressed in millimeters of mercury. Each *point* represents the mean value ± standard error of the mean. $^*p < 0.0001$ at each time after transplantation compared with before transplantation for Pao_2.

Table III. *Comparison of variables between patients free from OB (group 1, n = 10) and with OB (group 2, n = 5)*

Variable	*Group 1 n = 10*	*Group 2 n = 5*	*p Value*
Recipient age (yr)	46.53 ± 11.27	36 ± 11.1	0.09 NS
Donor age (yr)	25.84 ± 6.88	25 ± 8.37	0.8 NS
Donor ICU stay (hr)	25.88 ± 10.9	37.6 ± 20.5	0.13 NS
Cold ischemia (min)	253.07 ± 51.18	243.6 ± 28.0	0.7 NS
Bypass time (min)	202.3 ± 43.76	217.02 ± 48.5	0.5 NS
Mechanical ventilation (day)	2.04 ± 1.06	1.60 ± 0.89	0.4 NS
Early acute rejection	1 ± 1	1 ± 1	0.6 NS
Mean follow-up (mo)	34.5	47.2	
Late graft patency (%)	71.4	0	
Late acute rejection	0.31 ± 0.48	1.31 ± 0.95	0.02
CMV disease	0.38 ± 0.65	1.8 ± 1.3	0.006
Bronchitis	1.69 ± 0.95	5.8 ± 2.49	0.0008
Total infection episodes	4.54 ± 2.44	10.4 ± 5.13	0.004

OB, Obliterative bronchiolitis; *ICU,* intensive care unit; *CMV,* cytomegalovirus; *NS,* not significant.

ever the technique of DLT used, functional results of bilateral transplantation are obviously better.[23]

With regard to the choice of the conduit used for revascularization, the saphenous vein graft is easy and safe to use. It is likely to provide an excellent immediate blood supply, because the fish-mouth shaped distal anastomosis of the graft allows it to cover as many orifices of bronchial arteries as needed and thus ensures an optimal revascularization. But the internal thoracic artery, as advocated by Yacoub, Daly, and Pettersson, is well known to provide a more lasting blood supply than a venous graft. There is a better size concordance between thoracic artery and bronchial arterial runoff. Moreover, the physiologic ability of the arterial conduit to respond to changes in flow requirements with ap-

propriate vasodilation and constriction explains its capability to remain patent when anastomosed to small vessels. In the same situation, a venous graft is more likely to be thrombosed. Consequently, the internal thoracic artery should certainly be considered as the conduit of choice for this purpose. When considering the only immediate aim of airway healing, however, an early bronchial arterial revascularization success lasting 2 or 3 weeks appears to be sufficient for providing excellent airway healing.

With regard to long-term functional results, the effects of long-lasting revascularization remain to be explored. It is unlikely that revascularization could have an impact on alloimmune responses, because transplantation of vascularized organs such as kidney, liver, or heart does not prevent chronic rejection. However, after lung transplantation, lung physiology is greatly impaired. Several factors such as bronchial denervation and devascularization, as well as reperfusion injury, may have a role in the modification of mucociliary clearance and the structure and function of the bronchial epithelium.[24-26] Some of these factors could recover partially during the late postoperative period.[27] However, all these factors, as well as immunologic reactions and infections, can be involved in the pathogenesis of OB. Because these possible pathogenetic factors cannot be identified and checked separately in human transplantation, it was attractive to assess whether or not long-lasting revascularization could have a beneficial impact on lung function. It is certainly speculative, but also quite possible, that late patent bronchial arterial revascularization could participate in restoring physiologic conditions such as bronchial epithelium near to normal, with improved mucosal trophicity and mucociliary function. Maintenance of these functions could contribute to host defense against infection.[25]

OB currently remains the main event limiting the long-term success of lung transplantation. Our overall OB incidence of 33% is not different from those reported in other publications[10] but has to be correlated with a 43-month mean follow-up. The hypothesis that long-lasting bronchial arterial revascularization could contribute to a decrease in OB occurrence follows from our findings in a limited series, with incomplete data, because the best way to survey graft patency through a noninvasive technique remains to be defined. Thus our hypothesis is obviously more a suggestion than a certainty. However, because there was, until now, no satisfactory answer to an efficient OB prevention, and because it also has not been proved that chronic ischemia, despite the mechanisms of collateral blood supply, was harmless and without side effects, it appeared to us that this field of clinical research was worth exploring. Finally, the definitive answer as to whether long-lasting revascularization could be a contributing factor of some importance can only be confirmed or invalidated by a larger clinical experience and a truly longer follow-up. This conclusion could emerge from the some groups using the long-lasting patent internal thoracic artery for bronchial arterial revascularization.

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Discussion

Dr. Shaf Keshavjee *(Toronto, Ontario, Canada).* The University of Bordeaux group are to be credited for the development of this truly simplified technique of bronchial arterial revascularization in which a saphenous vein graft is used and the distal anastomosis is performed on the back table. Bronchial arterial revascularization addresses two issues, the first being ischemia of the airway and the second being OB. Like most other transplant programs, we have found that airway ischemia is not as large a problem as it was in the past. For example, over the past 4 years or so in Toronto in the last 137 transplants, with 262 telescoped, nonrevascularized anastomoses "at risk," we have had eight patients (or a 3% incidence of stricture) requiring a dilatation and one patient (or a 0.4% incidence of stricture) requiring a stent. This improvement in airway healing is likely attributable to multiple factors including anastomotic technique and lung preservation. Thus, although the problem is not as large as it used to be, there still is room for improvement.

The major issue, then, is the role of bronchial arterial revascularization in the prevention of OB. In this series of 18 patients, the authors report an incidence of OB of 28%, which is not different from results from centers not performing bronchial arterial revascularization. Interestingly, however, all patients with OB had an occluded vein graft. My question is this: Which is the horse and which is the cart? Did the vein graft occlusion lead to OB or vice versa?

Finally, as the authors have indicated, OB is likely a multifactorial phenomenon. The situation of chronic relative ischemia wherein the transplanted lung bronchus is fed by pulmonary arterial blood, which is low in saturation and has a low perfusion pressure, may indeed be a significant contributing factor. However, I think that the only way we are going to be able to conclusively prove it is by performing a study of unilateral bronchial arterial revascularization in bilateral lung transplant recipients. Dr. Baudet, I would like to ask your opinion with respect to that sort of a study, in which case each patient would serve as his own control.

Dr. Baudet. Thank you for your comments. To answer your first question, despite our findings that OB did not develop in patients with a long-term patent venous graft, it could be asserted that rejection and infection associated with OB occurrence could impair the distal bronchial arterial bed, reduce the runoff, and thus might be responsible for graft occlusion. But our data were given just as findings suggesting a hypothesis, rather than being an assertion. If the 28% OB incidence in our series is not different from that of centers not performing bronchial arterial revascularization, it has to be correlated with a longer follow-up than in the other series. The longer the follow-up, the higher the OB incidence, which is more than 28% in reports with a follow-up longer than 5 years. With regard to your suggestion of one-lung revascularization in sequential bilateral lung transplantation so that the patient would act as his or her own control, this aim could be achieved by revascularization of the left lung with the internal thoracic artery, as performed by Yacoub, or of the right lung by direct anastomosis of the right intercostobronchial artery into the aorta. This may be a partial answer for the pathogenesis of this multifactorial disease.

Dr. Gosta Pettersson *(Copenhagen, Denmark).* We all recognize the pioneering work of the Bordeaux group in relation to direct bronchial arterial revascularization in lung transplantation. In Copenhagen we were convinced from the beginning that the beneficial effect of successful revascularization went beyond healing of the airway anastomosis; therefore we used the internal thoracic artery, as proposed by Yacoub, as a conduit. In Copenhagen we have performed, 53 DLTs, eight single-lung transplantations, and nine heart-lung transplantations with bronchial arterial revascularization. The 1- and 2-year survival of the DLTs is 82%. We have a 94% early patency of the bronchial arterial revascularization, and we have now reexamined 20 patients with primarily patent revascularization after 2 years. All 20 have patent bronchial arterial revascularization. Vascularity has even improved during that period.

Unfortunately, I am not able to confirm your observation that the incidence of OB syndrome should be exceptionally low with functioning revascularization. We have a 1-, 2-, and 3-year incidence of OB syndrome of 85%, 82%, and 67%, respectively. We have not yet correlated our OB syndrome results with the arteriographic findings.

I would like to ask you if you have done any grading of the success you have achieved with your revascularization? I would like you once again to come back with a suggestion about design of a study to confirm or exclude that revascularization makes a difference. I am in doubt about the suggestion of doing revascularization on one side and not the other. By chance we have had hemilaterally successful revascularization, and we have seen severe OB syndrome in both lungs for one of those patients. OB syndrome, per se, seems to be associated with increased vascularity rather than the opposite. That is a comment addressed to one of the previous questions.

Dr. Baudet. Thank you, Dr. Pettersson, for your comments. Your technique of revascularization using the internal thoracic artery, as proposed by Yacoub and also performed by Daly, is certainly the best way to achieve long-lasting revascularization. That is already confirmed by your experience. But your 2-year incidence of OB is somewhat disappointing. However, since this 45% incidence includes patients with primarily failed revascularization, these results, as you mentioned, have to be correlated with the results of arteriographic findings.

To answer your question, we have not done any revascularization grading but only a tracheal healing grading. However, revascularization using a venous graft, able to cover as many orifices of bronchial arteries as needed, is likely to provide a more complete bilateral revascularization, as demonstrated by our early and late angiographic studies. Nevertheless, because long-lasting revascularization is more frequently achieved when using the internal thoracic artery, the groups like yours, using this conduit, will be more able to answer this question. The best way to survey graft patency, whatever the conduit used, remains to be defined through noninvasive methods.

Dr. Joel D. Cooper *(St. Louis, Mo.).* There is no question that if you choose to do this en bloc operation, your revascularization technique is probably extremely important in reducing airway complications. However, my question is, why would you want to do this? If you consider your series overall, nothing in this series has accomplished anything better than has been reported by standard methods without revascularization. There is no lower hospital mortality rate; there is no reduction in overall incidence of OB; there is no reduction in deaths or complications from airway anastomoses. In the St. Louis Registry, which contains more than 4000 cases from around the world, the incidence of death from airway complications is 1% or less. Your technique does not reduce the incidence of OB or airway complications or improve either hospital survival or long-term survival. I would thus ask, as someone who has had the opportunity of performing both types of operations, why would you want to do an en bloc DLT, which is complicated and requires prolonged cardiopulmonary bypass, when the world experience at many centers has accomplished the same overall goals using a simpler type of transplant?

Dr. Baudet. Thank you, Dr. Cooper, for your comments and questions. The first aim of bronchial arterial revascularization was to improve airway healing because, at that time, the sequential technique was not yet used for bilateral lung transplantation; thus we have chosen to perform DLT with tracheal anastomosis.

In our opinion, for patients needing bilateral lung transplantation, the en bloc technique offered the advantages of reducing the duration of the operation and the donor organ ischemia, which can be very long for the second lung in sequential DLT. Because of a close collaboration between the Departments of Thoracic Surgery and of Cardiovascular Surgery, the en bloc technique, despite requiring cardiopulmonary bypass, which is in fact a very simple procedure, never appeared to be complicated or sophisticated or likely to induce short-term complications. The aim of our technique was to achieve a safe tracheal healing and, by this way, to reduce hospital mortality caused by airway dehiscence. In fact, in our series, there was no operative mortality, and the three hospital deaths were due to causes unrelated to tracheal complications or failed revascularization. With regard to late deaths, only two were due to OB, the three others being unrelated to the technique itself. Consequently, there were no early or late deaths attributable to tracheal complications. Concerning this point, in the 1996 St. Louis Registry, there was a 5% incidence of early deaths resulting from airway dehiscence, but long-term airway complications such as stricture or the need for stenting are not clearly reported. Finally, the 5% early and the 29% late death rates owing to OB/rejection were not correlated to the length of follow-up. Our 28% OB incidence was observed with a 43-month mean follow-up, ranging from 22 to 69 months. In the literature, with a such long follow-up, the current incidence of OB has been reported by the Stanford group to be 36% within the first 3 years, with an overall prevalence of 58% after heart-lung and 51% after lung transplantation.

I agree that the number of patients in our study is relatively small, and that any retrospective study can appear to be incomplete. However, since nobody, up to now, gave a satisfactory answer to OB prevention, it appeared to us that, in this multifactorial disease, the role of chronic lung and airway ischemia had to be explored. It is already obvious that improvement of mucosal trophicity and mucociliary clearance could play an indirect beneficial role. I hope that the final answer for this hypothesis can be given, for patients with a truly long follow-up, by the groups using for revascularization the long-lasting patent internal thoracic artery.